

AMENDMENTS TO THE DRAWINGS

Submitted herewith are three sheets of drawings including changes to Fig. 46. These sheets, which includes Fig. 46A-C, replace the original sheets including Fig. 46A-C. In Fig. 46, superfluous matter has been removed (e.g., shading, etc.) and truncated text has been corrected. Kindly substitute the enclosed formal drawings of Fig. 46A-C for the informal drawings of Fig. 46A-C filed on January 26, 2006.

Attachment: 3 Replacement Sheets

3 Annotated Sheets Showing Changes

COMMENTS ON STATEMENT OF REASONS FOR ALLOWANCE

Applicants hereby provide clarification of the language of the allowed claims by reference to the specification and prosecution history of the instant application.

Rodent hepadnavirus core antigen

The hybrid ground squirrel and woodchuck hepadnavirus particles of the allowed claims are those that assemble satisfactorily of Tables 11-13, 15 and 16, as correctly summarized in the Notice of Allowability mailed September 20, 2010. The amino acid sequences of *wild type* Woodchuck Hepadnavirus core Antigen “WHcAg” and *wild type* Ground Squirrel Hepadnavirus core Antigen “GSHcAg” are provided in SEQ ID NO:1 and 21, respectively. The majority of the hybrid WHcAg and GSHcAg of the allowed claims, however, **do not** possess wild type C-termini. Rather, the majority of the hybrid WHcAg and GSHcAg of the allowed claims are *truncated core antigens* of SEQ ID NOS:38 and 40 respectively, which further possess an *artificial C-terminus* of Table 1 and Table 3-1, respectively. The footnote of Table 1 indicates that “the wild type N-terminal [WHcAg] protein sequence (corresponding to positions 1-149) is set forth as SEQ ID NO:38,” while the footnote of Table 3-1 indicates that the “wild type N-terminal [GSHcAg] protein sequence (corresponding to positions 1-148) is set forth as SEQ ID NO:40.” Additionally, Example 8 of the Specification as filed discloses:

this expansion of the number of positions available for insertion of foreign epitopes was made possible by the generation of a library of C-terminal modifications to the WHcAg which variably stabilize insertions at different positions. In fact, the C-terminal modifications of the WHcAg described herein comprise a very useful second library of 21 C-terminal modifications. Table 1 lists the sequences of the various modified C-termini. The C-terminal modifications were designed to eliminate RNA/DNA binding motifs, eliminate/substitute prolines, replace the last five C-terminal amino acids and to eliminate or conserve non-homologous regions between HBcAg and WHcAg (US 2008/0131452, paragraph [0328]).

This teaching in combination with the summary indicates that the majority of the hybrid WHcAg and GSHcAg of the allowed claims possess an artificial C-terminus in place of the wild type C-terminus (e.g., not an artificial C-terminus following the wild type C-terminus as suggested by the Statement of Reasons for Allowance). Thus, for example, the HyW-M92 WHcAg of Tables sf-2931296

11, 12, 15 and 16 possesses the M heterologous antigen (SEQ ID NO:75) inserted at position 92 of a woodchuck platform having a “HyW” C-terminus (e.g., WHcAg = SEQ ID NO:38 N-terminus plus SEQ ID NO:15 C-terminus). Similarly, the HyW-M92 GSHcAg of Table 15 possesses the M-heterologous antigen (SEQ ID NO:75) inserted at position 92 of a ground squirrel platform having a “HyW” C-terminus (e.g., GSHcSg = SEQ ID NO:40 N-terminus plus SEQ ID NO:15 C-terminus).

Particles that assemble satisfactorily

In the Response submitted to the Office on July 20, 2010, Applicants indicated that the amended claims were directed to methods of producing an immune response by administration of “hybrid rodent particles with an assembly score of 3 or greater of Table 11, hybrid rodent particles described as assembling satisfactorily of Tables 12 and 13, hybrid rodent particles with a positive (+) assembly score of Table 15, and the purifiable hybrid rodent particles of Table 16 (e.g., > 2 mg/L)” (Response, page 5). Thus, particles that assemble satisfactorily comprise those that are marked with a “+” in Table 15, pages 122-123, with regard to both WHcAg and GSHcAg.

Amendments to the drawings

Replacement sheets (3) for Fig. 46A-C are hereby provided to remedy the drawing deficiencies noted in the Notice to File Corrected Application Papers mailed November 8, 2010. Applicants understand that all outstanding requirements are now satisfied by correction of the noted informalities by virtue of this submission.

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Respectfully submitted,

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Attachments

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